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REMARKS

New Claims

Applicants submit herewith a number of new claims directed to polypeptides and methods of use thereof which are directed to the polypeptides encoded by the polynucleotides previously examined herein. Applicants gratefully acknowledge the Examiner's having agreed to examine this related subject matter in the instant application, particularly in view of the long pendency of this application resulting from a number of circumstances, in particular the previous suspension of the allowed claims for over two years, followed by the new non-final rejection issued in view of the new Utility Examination Guidelines, as well as the paperwork mixup which resulted in the Examiner's reply to Applicants' After Final Response not being issued for over 8 months.

Specific support for the new claims can be found in the specification as filed, as follows:

- Claims 61 and 67 are supported throughout the specification, and are similar though not identical in scope, to claims 43 and 55, respectively.
- Claims 62-64 are supported in the specification, e.g., at pages 2-5 which describe the general mechanism of cytokines in leukocyte trafficking in inflammatory responses, as well as supported by the general knowledge in the art at the time the invention was made, e.g., as disclosed by the references cited in the background of the invention.
- Claims 65-66 are supported in the specification, e.g., on pages 2-3, and page 23.
- Claim 68-69 are supported in the specification, e.g., on page 3.
- Claims 70-75 are supported throughout the specification, e.g., pages 9, 13, 15 and 27.
- Claim 76-78 are supported throughout the specification, e.g. on page 20 and Figure 5, which disclose preferred fragments of the polypeptide of SEQ ID NO:4.
- Claim 79 is supported in the specification, e.g., on page 10.
- Claims 80-87 are supported throughout the specification, e.g., on pages 13 and 19-21, as well as supported by the general knowledge in the art at the time the invention was made, e.g., as disclosed by the references cited in the background of the invention, e.g., well known useful types of antibody subfragments and modifications of antibodies such as single chain and humanized antibodies and Fab and $F(ab)_2$ fragments.

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- Claims 88-90 are supported in the specification, e.g., on pages 21-22.
- Claims 91-96 are supported in the specification, e.g., on pages 19-21.
- Claims 97-98 are supported in the specification, e.g., on page 13, as well as supported by the general knowledge in the art at the time the invention was made, e.g., as disclosed by the references cited on page 13, e.g., well known techniques for making antibodies such as by screening libraries.
- Claims 99 and 101 are supported throughout the specification, e.g., on pages 21-22.
- Claim 100 is supported in the specification, e.g., on page 22.
- Claims 102-103 are supported throughout the specification, e.g., on pages 26-27.
- Claim 104 is supported throughout the specification, e.g., on pages 24-25.

The specific phraseology of new claims 63-75 is also generally supported throughout the specification, at e.g., page 2, last full paragraph, page 3, first full paragraph, paragraph bridging page 8, third and fourth paragraphs on page 13 the mentioned Examples, as well as Examples IX and XII:

The foregoing claims are not limited to the specific tissue mentioned in the application, i.e., the pancreas. This is because the specification is clearly directed to use of PANEC-1 and PANEC-2 in any tissue to which they relate, not only the pancreas. Note, for example, the first full paragraph on page 21 (Example X relating to diagnostic tests and antibodies) which states that "To date, PANEC -1 and PANEC-2 has been found only in the pancreas." This clearly inherently signals that other tissues can be involved in the invention. All of the discussion in the specification written in terms of the pancreas would automatically be recognized by a skilled worker as pertaining equally well to other tissues in which PANEC-1 and PANEC-2 are implicated.

Consistent with this fundamental fact is the formulation of examples XIII (drug screening), XIV (rational drug design), XV (PANEC 1 and PANEC-2 receptors) and XVI (use and administration of PANEC-1 and PANEC-2) in general terms not limited to the pancreas. Note especially in the discussion of the identification of receptors (Example XV), where a "library is transfected into a population of cells, and those cells expressing the receptor are selected ...". As well, note page 28, second paragraph: "It is anticipated that different formulations will be effective for different TECs and that administration targeting the pancreas may necessitate delivery in a manner different from that to another organ

or tissue." Furthermore, note that original claims 20, 21 and 23 are generic to pharmaceutical compositions with no limitation as to tissue type. The abstract is also not specific to any tissue type.

Thus, the invention is clearly disclosed to one of ordinary skill in the art as related to PANEC-1 and PANEC-2 and any tissue in which they are found.

Submission of Newly-Discovered Information

In preparation for submitting this Response, Applicants have recently reviewed a number of sources of publications relating to the instantly claimed sequences, and are submitting a number of documents herewith which relate to these sequences. Most of these submissions related to post-filed disclosures that further support Applicants' asserted utilities and additional uses for the claimed sequences, and are provided to complete the record.

Upon allowance of the instant claims, there should be no cause for any additional suspension

As noted above, the instant application was previously found allowable in 1998; however, at that time, the application was suspended for a potential interference with a not-as-yet allowed application. This suspension lasted for over two years. In 2000, the application was withdrawn from suspension by issuance of a new, non-final Office Action, in which a new rejection under § 101 was made. This rejection has since been withdrawn, and Applicants submit that the claims presented herein are again in condition for allowance. However, Applicants respectfully submit that, upon allowance of these claims, there should be **NO** suspension of the application, regardless of the status of the presumably still-not-as-yet allowed, potentially conflicting application, for the following reasons.

PANEC-2:

The Examiner's attention is directed to enclosed U.S. Serial Number 08/294,251, filed August 23, 1994, which is the priority document for PCT application WO 9606169, filed June 5, 1995. Applicants believe that a corresponding US application was the basis upon which the instant application was suspended for over two years after it was allowed, because it might eventually have allowable conflicting claims. Applicants wish to bring to the Examiner's attention the following facts and information:

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- The enclosed priority application U.S. Serial Number 08/294,251 (hereafter "the '251 application"), assigned to Human Genome Sciences, Inc., was obtained by Applicants from the Australian Patent Office, with which it is presumed to have been filed with the Australian National Stage filing of PCT application WO 9606169.
- The '251 application as received from the Australian Patent Office included **TWO** Sequence Listings, one apparently filed with the '251 application on its initial filing date, containing 2 sequences ("the first Sequence Listing") and a second Sequence Listing apparently filed at a later date, which contained 6 sequences ("the second Sequence Listing").
- In addition, there were two drawing figures provided with the application as received from the Australian Patent Office.
- The first Sequence Listing is numbered as pages 31-33 of the specification. On page 32 of the specification, SEQ ID NO:1 is disclosed as having 378 nucleotides; this is a **VERY** different polynucleotide sequence from that of PANEC-2 (SEQ ID NO:3) of the instant application. On page 33, the corresponding protein SEQ ID NO:2 is disclosed as having 125 amino acids; this is a **VERY** different amino acid sequence from that of PANEC-2 (SEQ ID NO:4) the instant application.
- On page 3 of the '251 specification, Figure 1 is described as displaying "the cDNA and corresponding deduced amino acid sequence of Ckβ-9" and that "[t]he initial 22 [sic: 23 from the originally filed, first Sequence Listing] amino acids represent the leader sequence such that the putative mature polypeptide comprises 102 amino acids." However, the Figure 1 attached to the document sent by the Australian Patent Office clearly does not reflect sequences of that length; instead, the sequences in this Figure 1 (presumably filed with or after the second Sequence Listing, as they are found after the second Sequence Listing at the end of the specification of '251 and after the Abstract) have, respectively 405 nucleotides and 134 amino acids.
- The second Sequence Listing submitted in the '251 application (no page numbers) has for SEQ ID NO:1 a **405** nucleotide sequence. This sequence differs from the first filed SEQ ID NO:1 in that there is a deletion of a "T" nucletotide at nucleotide 284, and the sequence continues for an additional 29 nucleotides past the end of the SEQ ID NO:1 listed in the first Sequence Listing.

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- The second Sequence Listing submitted in the '251 application (no page numbers) has for SEQ ID NO:2 a **134** amino acid sequence. This sequence differs from the first filed SEQ ID NO:2 in that there is a different amino acid at amino acid 85 (corresponding to amino acid 72 of the "mature" protein, according to the numbering in the Sequence Listing), a completely different sequence from amino acid 85 -115 (corresponding to amino acids 72-102 of the "mature protein, according to the numbering in the Sequence Listing), and the amino acid sequence continues for an additional 9 amino acids past the end of the SEQ ID NO:1 listed in the first Sequence Listing for a total of 134 amino acids.

Applicants respectfully submit that it is *prima facie* apparent that the first Sequence Listing filed in the '251 application did not disclose or even remotely support the polynucleotide or amino acid sequences disclosed in either the subsequently filed second Sequence Listing or subsequently filed Figure 1. It is submitted to be clear from the specification that the '251 application **as filed** was directed to a shorter and incorrect polynucleotide and amino acid sequence, which the Applicants of the '251 application attempted to correct by submitted a second Sequence Listing and Figure 1 which do not correspond to the sequences described in the specification.

The instant Applicants respectfully submit that the second Sequence Listing and apparent replacement Fig. 1 **clearly** were and are new matter to the '251 application as filed. If those replacement papers were allowed to be submitted in the '251 application (which Applicants cannot know, since neither that application nor any US application which claims priority to it have been issued by the USPTO, and thus the contents of its file history are presently unknown to Applicants), Applicants submit that they should not be given any consideration, and that any alleged priority claimed by the Applicants of the '251 application in this or any later-filed application as of the August 1994 filing date, including any CIP application correcting the sequences in accordance with the second Sequence Listing or the apparently later filed Figure 1, should be disallowed. To the instant Applicants' knowledge, the earliest priority date to which HGS is entitled for the full 134 amino acid sequence (and full 402 nucleotides encoding it [HGS counted the stop codon at the end to arrive at 405 nucleotides]) corresponding to the instant Applicants' 134 amino acid sequence and 402 nucleotides encoding it, is

June 5, 1995, which was the filing date of the PCT application WO 9606169 which designated the US, assuming that a corresponding US National Phase application is now pending before the USPTO.

Since a priority claim to the longer sequences as represented in the later filed second Sequence Listing and Figure 1 cannot properly be made based on the '251 application as filed, and the instant Applicants respectfully submit that the effective filing date of the instant application is more than three months prior to the effective filing date of the PCT application WO 9606169 (assuming it designated the US and assuming that a corresponding US National Phase application or proper continuation application claiming priority to that US National Phase application is now pending before the USPTO), Applicants further submit that, upon allowance of the claims of the instant application, the instant application should immediately issue as a US patent, as no suspension based upon the priority of the sequences **as filed** in the HGS '251 application would be proper.

At the very least, since the instant Applicants' allowable claims would be *prima facie* entitled to an effective filing date over 3 months prior to the effective filing date of any claims of HGS to the same or similar sequence, the instant Applicants submit that they should be entitled to be deemed the Senior Party, and their application should be allowed to issue, with the burden being shifted to HGS to make the necessary statements and affidavit under 37 C.F.R. § 1.608(b). See, e.g., M.P.E.P § 2303: "Interferences will not be declared between pending applications if there is a difference of more than 3 months in the effective filing dates of the oldest and the next oldest applications of a simple character ...". Applicants submit that the "simple character" requirement is met by the ease of comparing the sequences and the effective filing dates of each application. Therefore, there is no reason to delay issuance of the present claims directed to PANEC-2 based on the HGS application, if it is still pending.

PANEC-1:

Applicants note that US 6,403,782 was recently issued. Although it claims to relate to DNA sequences encoding human eotaxin and the polypeptide it encodes shares substantial sequence identity with PANEC-1, it is not identical to SEQ ID NO:2, nor is the nucleotide sequence it discloses identical with SEQ ID NO:1. Moreover, the earliest priority claimed by this patent is to an application filed June 22, 1995, over **four months** after the instant application was filed. Therefore, there should be no reason to suspend the issuance of the instant claims.

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In addition to the '782 patent, Applicants direct the Examiner's attention to the following patent applications, none of which appear to have resulted in issuance of a US patent. Nevertheless, in the interest of completing the record, this information is being disclosed to the Examiner.

- 95US-0494093 (assignee LeukoSite, now Millennium Pharmaceuticals), based on the priority claimed in PCT application publication WO 9700960): The claimed US priority application was apparently filed on June 23, 1995, over **four months** after the instant application was filed.
- 95JP-0259067 (assignee Shionogi Institute), based on priority claimed in PCT application publication WO 9712914: The claimed Japanese priority application was apparently filed on October 5, 1995, almost **eight months** after the instant application was filed.
- 99US-0261201 (assignee Human Genome Sciences, Inc.), based on priority claimed in a US patent application publication 2002026044, which application was filed March 3, 1999: Priority claimed in the 1999 HGS application is to a PCT patent application publication WO 96/05856, which is PCT application 94WO-US09484, filed on August 23, 1994, almost six months prior to the filing date of the instant application. However, the 1999 application discloses a shorter version of the PANEC-1 sequence, a 74 amino acid polypeptide lacking the N-terminus of the claimed sequence. Moreover, it appears that the 74 amino acid sequence was not disclosed at all in the 1994 application, a copy of which is submitted herewith

Both PANEC-1 and PANEC-2

Finally, the instant Applicants note that this case was deemed to be in condition for allowance **four (4) years ago**, and this application has been pending for **seven and one half (7-1/2) years**. . During this time, Applicants have been denied and continue to be denied the benefit of licensing opportunities for their proper claims to these sequences and inventions, which is causing the Assignee of the application financial harm. Therefore, the instant Applicants respectfully request that the claims of this application be immediately passed to issue upon finding that they are allowable and upon payment of the Issue Fee.

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Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has objected to the claims for the following reasons, which are addressed in the order presented:

a. Stringent hybridization conditions not disclosed

While Applicants disagree that the claims as recited were not supported, *ipsis verbis* or otherwise, in the specification, one of ordinary skill in the art would understand what is by stringent hybridization conditions reference to any number of primary textbooks, e.g., Sambrook et al. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY (see the specification at page 10, lines 10-11). This term was well understood in the art at the time the invention was made.

Nevertheless, in the interest of expediting prosecution of the instant claims, Applicants have now substituted different functional language (rather than hybridization conditions) to specify that sequences included within the metes and bounds of the claims are identifiable by comparing the sequences mathematically, i.e., wherein the sequence identity between the sequence in question and SEQ ID NO:1 is 90% or greater. Means for comparing sequence identify are similarly well known in the art, and furthermore are disclosed in various places in the specification, e.g., Example IV. In no way should this amendment be construed as narrowing the scope of the claims; in fact, if anything, the alternative functional language broadens the scope of the claims, as highly stringent hybridization conditions are less forgiving of sequential nucleotide changes.

Withdrawal of this rejection is therefore respectfully requested.

b. Genomic sequences not disclosed

Applicants respectfully submit that the instant claims do not encompass genomic polynucleotide sequences, which by definition include non-coding sequences encompassing the coding sequences as present in genomic (chromosomal) DNA. Rather, the claims are directed to purified polynucleotide sequences that directly encode the claimed polypeptide, without requiring excision of any intronic sequences or other non-coding sequences. Applicants respectfully submit that without disclosure of precisely which sequences are intronic and are thus to be eliminated in order to perform the function of encoding the functional polypeptide(s), genomic sequences cannot either render the claimed sequences obvious, nor can they reasonably be included within the scope of the polynucleotide claims. Rather, the

claimed polynucleotides encompass sequences that directly encode (codon by codon) the claimed polypeptide. Any other reading of the claim is strained, at best. This does not mean that any 5' or 3' extensions, in particular heterologous regulatory sequences, are not literally encompassed, but rather that no sequence containing intervening intronic sequences of any significance are encompassed.

Furthermore, the claims as amended to recite the mathematical method of defining (and thus evaluating) encompassed naturally occurring variants do not read on genomic sequence including introns.

For the record, since the claims did not read on naturally-occurring genomic sequences such as introns in the first place, this clarification should not be construed as in any way limiting or narrowing the scope of the claim with respect to the doctrine of equivalents.

Withdrawal of this rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Applicants first note that the objection to claim 53, regarding the alleged indefiniteness of "at least 20 contiguous nucleotides" in defining the probe to be used in the method of detection, is curious in light of the number of times this exact wording has been allowed throughout Technology Center 1600 in the past 2 years. Apparently, most Examiners have "assumed that these nucleotides are a segment from the target polynucleotide" (actually, a segment from a sequence complementary to said target polynucleotide), as has this Examiner, and have had no issue regarding whether that this reading is in any way vague or indefinite. Nevertheless, in the interest of expediting prosecution of the instant claims, Applicants have amended the phrase to define the nucleotide probe in terms of being a segment of a nucleotide sequence, which was its clear meaning without the amendment. Applicants expressly assert that this amendment is in no way a limitation, and do not intend any relinquishment or disclaimer of any subject matter, of the claimed invention.

As for the objection to claim 40, part b), Applicants note that the amendment to the claim substituting percent sequence identity for high stringency hybridization conditions to indicate the metes and bounds of the variant language also obviates this objection.

Withdrawal of these rejections is therefore respectfully requested.

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CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application, including the newly added claims, is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650) 845-4639.

Please charge Deposit Account No. **09-0108** in the amount of **$**_____ as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 40, 52 and 53 have been amended as follows:

40. **(Twice Amended.)** An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

a) a polynucleotide sequence encoding an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4,

b) a polynucleotide sequence encoding a naturally-occurring amino acid sequence 90% identical to an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 [which hybridizes under stringent conditions to the full length of a)],

c) a polynucleotide sequence fully complementary along its length to a),

d) a polynucleotide sequence fully complementary along its length to b), and

e) a ribonucleotide equivalent of a)-d).

52. **(Twice Amended.)** An isolated polynucleotide comprising a sequence selected from the group consisting of:

a) a polynucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3,

b) a naturally-occurring polynucleotide sequence 90% identical to a polynucleotide of SEQ ID NO:1 or SEQ ID NO:3 [which hybridizes under stringent conditions to the full sequence of a)],

c) a polynucleotide sequence fully complementary along its length to a),

d) a polynucleotide sequence fully complementary along its length to b), and

e) a ribonucleotide equivalent of a)-d).

53. **(Twice Amended.)** A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 52, the method comprising:

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a) hybridizing the sample with a probe comprising a segment of at least 20 contiguous nucleotides[, said probe comprising] of a polynucleotide having a sequence complementary to said target polynucleotide in the sample, [and which] wherein said probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof; wherein the amount of hybridization complex corresponds to the amount of target polynucleotide in the sample.

Claims 61-104 have been added as follows:

61. **(New.)** An isolated polypeptide selected from the group consisting of:

z) a polypeptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4,

aa) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4,

bb) a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4, and

cc) an immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

62. **(New.)** A method of inducing an immune response, comprising administering to a patient in need of such treatment an immune-response inducing amount of a polypeptide of claim 61.

63. **(New.)** A method of inducing an immune response, comprising administering to a patient in need of such treatment an immune-response inducing amount of a polypeptide of claim 44.

64. **(New.)** A method of inducing an immune response, comprising administering to a patient in need of such treatment an immune-response inducing amount of a polypeptide of claim 45.

65. **(New.)** A method of claim 62, wherein the immune response is a chemotactic response in a leukocyte.

66. **(New.)** A method of claim 65 wherein said response is chemoattractive.

67. **(New.)** A composition comprising a polypeptide of claim 61 and an acceptable excipient.

68. **(New.)** A method of treating inflammation or disease mediated by a polypeptide of claim 61, comprising administering an antibody, an inhibitor, or a receptor specific to said polypeptide.

69. **(New.)** A method of treating inflammation or disease mediated by a polypeptide of claim 61, comprising administering an agonist or antagonist thereof.

70. **(New.)** A method of treating inflammation or disease mediated by a polypeptide of claim 61, comprising administering an antibody to a receptor specific to said polypeptide.

71. **(New.)** A method of claim 71, wherein said antibody is monoclonal.

72. **(New.)** A method of treating excessive production of a polypeptide of claim 61, comprising administering an antibody, inhibitor, receptor or antagonist thereof.

73. **(New.)** A method of treating excessive production of a polypeptide of claim 61, comprising administering an antibody to a receptor specific to said polypeptide.

74. **(New.)** A method of claim 69, wherein said disease is a viral or bacterial infection, injury associated with trauma, hereditary disease, infiltrative disease, leukemia or lymphoma.

75. **(New.)** A method of claim 69, wherein the disease is a disease of the pancreas.

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76. **(New.)** A polypeptide comprising a fragment of a polypeptide claim 45 from amino acid 79 to amino acid 134.

77. **(New.)** A polypeptide comprising a fragment of a polypeptide claim 45 from amino acid 105 to amino acid 134

78. **(New.)** A polypeptide comprising a fragment of a polypeptide claim 45 from amino acid 79 to amino acid 105.

79. **(New.)** A method of making a recombinant polynucleotide of claim 46, wherein the polynucleotide encodes a polypeptide of SEQ ID NO:4, comprising operably linking a polynucleotide encoding a polypeptide of SEQ ID NO:4 to promoter sequence, whereby the resulting recombinant polynucleotide is capable of being expressed in a host cell.

80. **(New.)** An isolated antibody which specifically binds to a polypeptide of claim 61.

81. **(New.)** An isolated antibody of claim 80 which specifically binds to a polypeptide having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

82. **(New.)** An isolated antibody of claim 81, wherein said polypeptide has a sequence of SEQ ID NO:2.

83. **(New.)** An isolated antibody of claim 81, wherein said polypeptide has a sequence of SEQ ID NO:4.

84. **(New.)** The antibody of claim 81, wherein the antibody is:

a) a chimeric antibody,

b) a single chain antibody,

c) a Fab fragment,

d) a F(ab')$_2$ fragment, or

e) a humanized antibody.

85. **(New.)** A composition comprising an antibody of claim 81 and an acceptable excipient.

86. **(New.)** A composition comprising an antibody of claim 82 and an acceptable excipient.

87. **(New.)** A composition comprising an antibody of claim 83 and an acceptable excipient.

88. **(New.)** A method of diagnosing a condition or disease associated with the expression of a polypeptide having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 in a subject, comprising administering to said subject an effective amount of the composition of claim 85.

89. **(New.)** A composition of claim 85, wherein the antibody is labeled.

90. **(New.)** A method of diagnosing a condition or disease associated with the expression of a polypeptide having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 in a subject, comprising administering to said subject an effective amount of the composition of claim 89.

91. **(New.)** A method of preparing a polyclonal antibody with the specificity of the antibody of claim 81, the method comprising:

a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4, or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibodies from said animal, and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

92. **(New.)** An polyclonal antibody produced by a method of claim 91.

93. **(New.)** A composition comprising the polyclonal antibody of claim 92 and a suitable carrier.

94. **(New.)** A method of making a monoclonal antibody with the specificity of the antibody of claim 81, the method comprising:

a) immunizing an animal with a polypeptide consisting of an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4, or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibody producing cells from the animal,

c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells,

d) culturing the hybridoma cells, and

e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

95. **(New.)** A monoclonal antibody produced by a method of claim 94.

96. **(New.)** A composition comprising the monoclonal antibody of claim 95 and a suitable carrier.

97. **(New.)** The antibody of claim 81, wherein the antibody is produced by screening a Fab expression library.

98. **(New.)** The antibody of claim 81, wherein the antibody is produced by screening a recombinant immunoglobulin library.

99. **(New.)** A method of detecting a polypeptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 in a sample, the method comprising:

a) incubating the antibody of claim 81 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 in the sample.

100. **(New.)** A method of purifying a polypeptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 from a sample, the method comprising:

a) incubating the antibody of claim 81 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) separating the antibody from the sample and obtaining the purified polypeptide comprising an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

101. **(New.)** A diagnostic test for a condition or disease associated with the expression of a polypeptide having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4 in a biological sample, the method comprising:

a) combining the biological sample with an antibody of claim 81, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex, and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

102. (New.) A method of purifying a receptor for a polypeptide of claim 61, comprising

a) contacting a polypeptide of claim 61 bound to a support with a sample comprising an extract of receptor-bearing cells, under conditions where receptor binds to the polypeptide,

b) recovering and isolating the receptor bound to the polypeptide.

103. (New.) A method of claim 102 for cloning the receptor, further comprising

c) partially sequencing the receptor isolated in step b),

d) designing degenerate probes to the sequence identified in step c),

e) cloning the receptor gene.

104. (New.) A method of screening for a compound that modulates the activity of the polypeptide of claim 61, the method comprising:

a) combining the polypeptide of claim 61 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 61,

b) assessing the activity of the polypeptide of claim 61 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 61 in the presence of the test compound with the activity of the polypeptide of claim 61 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 61 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 61.